# HepaRegeniX Receives Orphan Drug Designation for Darizmetinib for the Prevention of Post-Hepatectomy Liver Failure

*U.S. FDA Orphan Drug Designation underscores darizmetinib's potential to address a significant unmet need following liver resection*

**Tuebingen, Germany, August 26, 2026** – HepaRegeniX GmbH ("HepaRegeniX"), a clinical-stage biotech company advancing novel therapies for acute and chronic liver diseases, today announced that the U.S. Food and Drug Administration (FDA) has granted Orphan Drug Designation (ODD) to darizmetinib (formerly HRX215) for the prevention of post-hepatectomy liver failure. Darizmetinib is a selective inhibitor of mitogen-activated protein kinase kinase 4 (MKK4), a key regulator of liver regeneration, designed to accelerate and enhance the liver's natural regenerative capacity in both healthy and diseased liver tissue.

"Post-hepatectomy liver failure is a serious and potentially life-threatening complication of liver resection and can limit the ability of patients to recover following extensive resection. With no approved treatment for these patients, there is a clear need for new therapeutic approaches," said **Linda Greenbaum, Chief Medical Officer of HepaRegeniX.** "Darizmetinib is designed to enhance the liver's regenerative capacity and support recovery when the remaining liver may not have sufficient capacity to regenerate and maintain essential function following surgery."

"Receiving the Orphan Drug Designation for darizmetinib is an important regulatory milestone for HepaRegeniX and supports its continued development for patients undergoing liver resection," said **Elias Papatheodorou**, **Chief Executive Officer of HepaRegeniX.** "As we advance darizmetinib into later-stage clinical development, the designation strengthens our ongoing engagement with the FDA and advances our goal of bringing a new treatment option to patients."

The designation follows completion of the initial part of the Phase Ib/IIa study (NCT06638502) in patients undergoing minor liver resection, in which darizmetinib demonstrated favorable tolerability and pharmacokinetic profiles. The second part of the study is expected to begin in the third quarter of 2026 and will evaluate the safety and pharmacokinetics of darizmetinib in patients undergoing major liver resection.

The FDA grants Orphan Drug Designation to drugs and biologics that are intended to prevent, diagnose, or treat rare diseases or conditions affecting fewer than 200,000 people in the United States. The designation qualifies sponsors for certain incentives such as tax credits for qualified clinical trials, exemption from user fees, and regulatory guidance throughout development. The approved product will be entitled to seven years of post-approval market exclusivity in the U.S. for the disease for which it has the Orphan Drug Designation.

**About Darizmetinib (HRX215) and Liver Regeneration**

For patients with colorectal cancer liver metastases (CRLM) and other cancers affecting the liver, surgical resection remains the most effective potentially curative treatment. Successful liver resection depends on the ability of the remaining liver, known as the future liver remnant (FLR), to sustain essential functions and regenerate. When the FLR is insufficient in volume or function, the risk of post-

operative liver failure increases significantly, rendering many patients ineligible for potentially curative surgery.

Darizmetinib (formerly HRX215) is an orally or intravenously available small molecule inhibitor of mitogen-activated protein kinase kinase 4 (MKK4), a key regulator of liver regeneration. In preclinical models, darizmetinib has been shown to selectively inhibit MKK4, stabilizing and protecting hepatocytes while accelerating and enhancing regenerative processes, even in compromised or diseased livers. This therapeutic approach, currently explored in a Phase Ib/IIa trial (NCT06638502), could expand surgical eligibility to patients requiring extended liver resection who would otherwise be deemed inoperable, offering a new path to potentially lifesaving treatment. Darizmetinib has the potential to transform liver transplantation by preventing liver failure after the transplant of small liver grafts, thereby expanding living donor transplantation and offering novel therapeutic approaches for acute and chronic liver diseases with limited therapeutic options.

**About HepaRegeniX GmbH**
HepaRegeniX is advancing therapies to treat acute and chronic liver diseases based on groundbreaking discoveries of a novel cellular target and small molecules that enable rapid liver regeneration. We do so by harnessing the liver's inherent regenerative power not only in healthy but also in diseased livers. HepaRegeniX's lead candidate, darizmetinib (HRX215), is an orally available small molecule that selectively inhibits mitogen-activated protein (MAP) kinase kinase 4 (MKK4), a master regulator of liver regeneration. Building on demonstrated safety in clinical trials, HepaRegeniX is advancing darizmetinib in a Phase 1b/2a trial to prevent post-hepatectomy liver failure, with potential applications in living donor liver transplantation and severe alcohol-associated hepatitis. Beyond liver diseases, the company is also developing HRX233 in oncology.

HepaRegeniX is backed by experienced life science investors, including Vesalius Biocapital IV, Novo Holdings A/S, Boehringer Ingelheim Venture Fund (BIVF), Coparion, High-Tech Gründerfonds, Ascenion GmbH and Wellington Partners.

Visit our website at www.heparegenix.com to learn more about the company.

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